REMARKS

The Pending Claims

After entry of the requested amendments, claims 48, 51-57, 60-61, 65-69, 73-76, 81 and 88-98, 100-102, and 105-106 will be pending in this application.

Applicants have amended claim 48, pagagraph (c), as the Examiner has suggested, to recite that the nucleic acid molecule encodes a polypeptide that is present in plant cells in starch granule-bound form as well as soluble form and that is involved in the phosphorylation of starch when expressed in plants and/or that increases the phosphorylation of glycogen when expressed in *E. coli*. Support for this amendment may be found, for example, on page 4, lines 1-3; page 8, lines 7-16; and page 46, lines 16-18.

Applicants have amended claims 51, 53, 54, 60, 65 and 68 to delete their reference to canceled claims. Applicants have amended claims 100 and 105 to depend from claims 48 and 102, respectively, due to cancellation of the intervening claims.

Applicants have amended claim 61 to recite the step of introducing the DNA molecule of claim 48 into the cell. Support for this amendment may be found, for example, on page 9, lines 16-22; and page 12, lines 17-29.

Applicants have amended claim 102, paragraph (c) to recite "more than 80% sequence identity . . . "; claim 105 to recite "more than 90% sequence identity . . . "; and claim 106 to recite "at least 95% complementarity . . . ." Support for these amendments may be found, for example, on page 5, lines 30-33; and page 9, lines 33-36.

None of these amendments adds new matter. Their entry is requested.

Applicants' October 17, 2002 Response

Applicants acknowledge with appreciation the Examiner's withdrawal of many of the previous rejections.

Specifically, the Examiner has withdrawn: (1) the objection to the specification; (2) the rejection of claims 48 and 60 under 35 U.S.C. § 101 as directed to non-statutory subject matter; (3) the rejection of claims 49, 51-57 and 60 under 35 U.S.C. § 112, second paragraph, as indefinite; (4) the rejection of claims 48, 51-54, 60-62, 68-69, 73-76, 81 and 88-95 under 35 U.S.C. § 102(b), as anticipated by Kull et al., "Genetic Engineering of Potato Starch Composition: Inhibition of Amylose Biosynthesis in Tubers from Transgenic Potato Lines by the Expression of Antisense Sequences of the Gene for Granule-bound Starch Synthase," J. Genet. & Breed., 49: 69-76 (1995) ("Kull"); (5) the rejection of claims 73 and 92-93 under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over St.-Pierre et al., "The Starch Phosphorylase Gene Is Subjected to Different Modes of Regulation in Starch-containing Tissues of Potato," Plant Molec. Biol., 30: 1087-1098 (1996); and (6) the rejection of claims 48-49, 51-57, 60-63, 65-69, 73-76, 81 and 88-95 under 35 U.S.C. § 103(a) as unpatentable over Kull taken with Bird et al., United States Patent 6,013,861.

The Pending Rejections

The Rejections Under 35 U.S.C. § 112, First Paragraph

New Matter

The Examiner has rejected added claims 104-106 under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the

claimed invention at the time the application was filed, i.e., for lack of written description. Specifically, the Examiner contends that claims 103-106 are drawn to certain percentages of sequence identity and that the specification fails to provide support for the language recited in the claims.

As described above and as suggested by the Examiner, applicants have canceled claim 104 and amended claims 105 and 106 to recite "more than 80% sequence identity," "more than 90% sequence identity," and "at least 95% complementarity," respectively, thereby obviating the rejection.

Enablement

The Examiner has maintained the rejection of claims 48, 51-57, 60-62, 65-69, 73-76, 81 and 88-95, and rejected added claims 96-106, under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner contends that the specification provides little guidance as to the function of the protein encoded by the claimed nucleic acid molecules. The Examiner states that applicants' submission of Ritte et al., "The starch-related R1 protein is an α-glucan water dikinase," Proc. Natl. Acad. Sci. USA 99:7166-71 (2002) ("Ritte") is inapposite because Ritte was published after the filing date. The Examiner further alleges that Ritte provides a characterization of the protein that contradicts applicants' assertion that the specification provides a functional description of the encoded protein. Applicants traverse.

As a preliminary matter, applicants note that Ritte was referred to in the October 17, 2002 response not as support for enablement of the claimed invention, but merely to indicate the enzymatic mechanism of the R1 protein. Further, the characterization

of the R1 protein in Ritte is entirely consistent with the characterization of the protein in the specification. The α-glucan water dikinase activity of the R1 protein described in Ritte results in the phosphorylation of both starch and glycogen. See abstract (copy of Ritte enclosed). Throughout the specification, applicants clearly indicate that expression of the R1 protein leads to the production of starch with increased phosphate content in plants and increased phosphorylation of glycogen in *E. coli*. See, e.g., page 4, lines 1-3; and page 8, lines 7-16.

The specification also teaches that the protein encoded by the claimed nucleic acid molecules has this function, namely that the additional expression of the protein in plants or *E. coli* results in the increased phorphorylation of starch or glycogen, respectively. See, e.g., page 4, lines 1-3; page 8, lines 7-16; page 13, lines 27-32; and page 51, line 30 to page 52, line 3. The specification also provides guidance for evaluating the ability of the claimed nucleic acid molecules in antisense orientation to reduce the amount of protein in plants and demonstrates that such plants produce starch with reduced phosphate. See, e.g., page 11, line 32 to page 12, line 8; Example 8, e.g., Tables 4 and 5; and Example 13, e.g., Table 7. Further, the specification provides enzymatic assays to assess whether a protein or fragment thereof phosphorylates glycogen in *E. coli*. See, e.g., page 4, lines 1-3; and Example 9. Thus, one of ordinary skill in the art, provided with the disclosure of this application, would clearly recognize that applicants have taught the function of the R1 protein, namely its phosphorylating activity. Further, one of ordinary skill in the art would be able to evaluate, without undue experimentation, whether fragments of the recited nucleic acid molecules encode a protein with this activity and whether such fragments, when expressed in antisense orientation in a plant cell, alter the properties of

starch produced in the plant cell, including the phosphate content of the starch. Thus, claims 48, 51-57, 60-62, 65-69, 73-76, 81, 88-95, and 96-106 are enabled by the specification.

The Examiner also contends that the recitation of "stringent [hybridization] conditions" in the claims encompasses low or moderately stringent conditions. According to the Examiner, such conditions would recover nucleic acid molecules encoding a multitude of unrelated proteins. The Examiner suggests amending the claims to recite "highly stringent conditions" or, alternatively, to amend claim 48, paragraph (c) to recite that the nucleic acid molecule of (c) encodes a polypeptide that is present in plant cells in starch granule-bound form as well as in soluble form and that is involved in the phosphorylation of starch when expressed in plants and/or that increases the phosphorylation of glycogen when expressed in *E. coli*. As described above, applicants have amended claims 48, paragraph (c) according to the Examiner's alternate suggestion, thereby obviating the rejection.

The Examiner maintains that the references cited in the July 19, 2002 Office Action teach the unpredictability of antisense RNA-mediated alteration of starch structure in plants. According to the Examiner, applicants' arguments fail to overcome this evidence of unpredictability in view of the lack of guidance with respect to evaluating fragments as short as 15 basepairs or with respect to nucleic acid variants that "hybridize" to the recited nucleic acid sequences or that have less than 80% sequence identity thereto. Applicants traverse this rejection in view of the claims as amended.

Applicants have amended claim 48, paragraph (c) to recite that the hybridizing nucleic acid molecule encodes a polypeptide that is present in plant cells in starch granule-bound form as well as soluble form and that is involved in the phosphorylation of starch when expressed in plants and/or that increases the phosphorylation of glycogen when expressed in *E. coli*. Applicants have amended claim 102, paragraph (c) to recite that the nucleic acid molecule has more than 80% sequence identity. Applicants also have canceled claim 99, which recited "[t]he DNA molecule of claim 48, wherein the DNA molecule is at least 15 basepairs and less than 2500 basepairs." Applicants expressly reserve the right to pursue the canceled subject matter in subsequent application(s) claiming priority herefrom.

As discussed above, the specification clearly teaches methods for identifying the nucleic acid molecules recited in the instant claims. For example, the specification teaches methods of determining whether a nucleic acid molecule encodes a polypeptide that is present in plant cells in starch granule-bound form as well as soluble form and that is involved in the phosphorylation of starch when expressed in plants and/or that increases the phosphorylation of glycogen when expressed in *E. coli*. See, e.g., page 4, lines 1-3; page 8, line 7-16; and page 46, lines 16-18. The specification also teaches that antisense RNA molecules may be used to reduce the expression of the R1 protein in plant cells, thereby resulting in changes to the physical and chemical properties of the starch produced in the cells. See, e.g., page 11, line 32 to page 12, line 8. The specification teaches that in order to efficiently cause an antisense effect, the DNA molecules encoding the antisense RNAs have a length of at least 15 nucleotides, preferably at least 100 or more than 500 nucleotides, as instantly claimed. See, e.g., page 9, lines 33-36 and page 12, lines 29-33.

The specification also teaches methods of determining whether a nucleic acid molecule recited in the claims is able to reduce phosphorylation of starch in plant cells when expressed in antisense orientation. See, e.g., page 33, line 15 to page 34, line 10; Example 8; and Example 13. Thus, one of ordinary skill in the art would reasonably expect RNA molecules encoded by the claimed DNA molecules to exert an antisense effect.

Finally, the Examiner contends that claim 61 is drawn to any method for reducing gene expression, including ribozyme methods. The Examiner states that claim 61 does not recite that plant transformation is involved in the reduction or that a particular nucleic acid molecule is used to cause the reduction.

Applicants have amended claim 61 to recite the step of introducing the DNA molecule of claim 48 into the plant cell and to incorporate the limitation of claim 62 that the reduction is due to an antisense effect, thus obviating the rejection.

Written Description

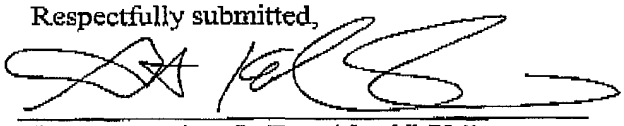
The Examiner has maintained the rejection of claims 48, 51-57, 60-62, 65-69, 73-76, 81 and 88-95, and rejected added claims 96-106, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. The Examiner questions the function of the encoded protein. The Examiner further states that applicants have not identified any particular regions in the protein which are conserved or which are responsible for the enzymatic function of the proteins. Applicants traverse.

As discussed above, the specification clearly teaches the function of the protein encoded by the nucleic acid molecules recited in the instant claims as well as how to make and use them. See, e.g., page 5, lines 3-13; Examples 6-8; and page 50, line 11 to page 52, line 14. Also as described above, the specification also teaches that expression of the nucleic acid molecules in a plant cell results in the production of modified starch and provides guidance for determining whether the nucleic acid molecules recited in the claims alter the amount of protein and thereby starch properties, including phosphorylation of starch, when expressed in antisense orientation in plants. Thus, contrary to the Examiner's assertion, one skilled in the art would clearly recognize that applicants were in possession of the invention as claimed.

Conclusion

For all of the reasons presented above, applicants request that the Examiner allow claims 48, 51-57, 60-61, 65-69, 73-76, 81 and 88-98, 100-102, and 105-106 to issue.

Respectfully submitted,



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Copy of claims 48, 51, 53, 54, 60, 61, 65, 68, 100, 102 and 105-106
marked up pursuant to 37 C.F.R. § 1.121(c)(1)(ii) to show changes made

48. (Three Times Amended) An isolated DNA molecule encoding an antisense-RNA complementary to a transcript of a nucleic acid molecule encoding a protein which is present in plant cells in starch granule-bound form as well as in soluble form and that is involved in the phosphorylation of starch when expressed in plants and/or that increases the phosphorylation of glycogen when expressed in *E. coli*, said nucleic acid molecule selected from the group consisting of:

(a) a nucleic acid molecule comprising a nucleotide sequence that encodes a protein having the amino acid sequence of SEQ ID NO: 2;

(b) a nucleic acid molecule comprising the coding region of the nucleotide sequence of SEQ ID NO: 1;

(c) a nucleic acid molecule that hybridizes to the nucleic acid molecule of (a) or (b) under stringent conditions, wherein the nucleic acid molecule encodes a polypeptide that is present in plant cells in starch granule-bound form as well as soluble form and that is involved in the phosphorylation of starch when expressed in plants and/or that increases the phosphorylation of glycogen when expressed in *E. coli*;

(d) a nucleic acid molecule the sequence of which is degenerate as a result of the genetic code to a nucleic acid molecule of (a), (b) or (c); and

(e) a fragment or allelic variant of a nucleic acid molecule of (a), (b), (c), or (d), wherein the fragment or allelic variant encodes a polypeptide that is present in plant

cells in starch granule-bound form as well as in soluble form and that is involved in the phosphorylation of starch when expressed in plants and/or that increases the phosphorylation of glycogen when expressed in *E. coli*,

wherein said antisense-RNA is capable of inhibiting the expression of nucleic acid molecules encoding said protein when expressed in a plant cell.

51. (Three Times Amended) A vector comprising the DNA molecule according to claim 48 [or 99].

53. (Three Times Amended) A host cell comprising the DNA molecule according to claim 48 [or 99] or comprising a vector comprising said DNA molecule.

54. (Three Times Amended) A transgenic plant cell comprising the DNA molecule according to claim 48 [or 99], wherein said DNA molecule is operably linked to regulatory elements ensuring transcription in a plant cell.

60. (Twice Amended) An RNA molecule obtainable by transcription of the nucleic acid molecule according to claim 48 [or 99].

61. (Three Times Amended) A method for producing a transgenic plant cell synthesizing a modified starch comprising the step of introducing the DNA molecule of claim 48 into the cell, thereby reducing in the cell the amount of a protein which is present in the plant cell in starch granule-bound form as well as in soluble form and that is involved in the phosphorylation of starch when expressed in plants and/or that increases the phosphorylation of glycogen when expressed in *E. coli*, said protein encoded by a nucleic acid molecule selected from the group consisting of:

(a) a nucleic acid molecule encoding a protein with the amino-acid sequence indicated in SEQ ID NO: 2;

(b) a nucleic acid molecule comprising the coding region of the nucleotide sequence indicated in SEQ ID NO: 1;

(c) a nucleic acid molecule hybridizing to a nucleic acid molecule of (a) or (b) under stringent conditions;

(d) a nucleic acid molecule the sequence of which is degenerate as a result of the genetic code to a nucleic acid molecule of (a) or (b); and

(e) a fragment, derivative or allelic variant of a nucleic acid molecule of (a), (b), (c), or (d), wherein the fragment, derivative or allelic variant encodes a polypeptide that is present in plant cells in starch granule-bound form as well as in soluble form and that is involved in the phosphorylation of starch when expressed in plants and/or that increases the phosphorylation of glycogen when expressed in *E. coli*;

wherein said reduction of the amount of said protein is caused by an antisense effect and results in the plant cell producing a modified starch.

65. (Three Times Amended) The method of claim 61 [or 62], wherein the enzyme activity of at least one further enzyme involved in the starch biosynthesis and/or modification is reduced.

68. (Three Times Amended) A plant cell obtainable by the method of claim 61 [or 62].

100. (Amended) The DNA molecule of claim [99] 48, wherein the DNA molecule is more than 100 basepairs.

102. (Amended) An isolated DNA molecule encoding an antisense-RNA complementary to a transcript of a nucleic acid molecule encoding a protein which is present in plant cells in starch granule-bound form as well as in soluble form and that is involved in the phosphorylation of starch when expressed in plants and/or that increases the phosphorylation of glycogen when expressed in *E. coli*, said nucleic acid molecule selected from the group consisting of:

(a) a nucleic acid molecule comprising a nucleotide sequence that encodes a protein having the amino acid sequence of SEQ ID NO: 2;

(b) a nucleic acid molecule comprising the coding region of the nucleotide sequence of SEQ ID NO: 1;

(c) a nucleic acid molecule that has [at least 40%] more than 80% sequence identity to the nucleic acid molecule of (a) or (b);

(d) a nucleic acid molecule the sequence of which is degenerate as a result of the genetic code to a nucleic acid molecule of (a), (b) or (c); and

(e) a fragment or allelic variant of a nucleic acid molecule of (a), (b), (c), or (d), wherein the fragment or allelic variant encodes a polypeptide that is present in plant cells in starch granule-bound form as well as in soluble form and that is involved in the phosphorylation of starch when expressed in plants and/or that increases the phosphorylation of glycogen when expressed in *E. coli*,

wherein said antisense-RNA is capable of inhibiting the expression of nucleic acid molecules encoding said protein when expressed in a plant cell.

105. (Amended) The DNA molecule of claim [104] 102, wherein the nucleic acid molecule of (c) has [at least] more than 90% sequence identity to the nucleic acid molecule of (a) or (b).

106. (Amended) The DNA molecule of claim 105, wherein the nucleic acid molecule of (c) has at least 95% [sequence identity] complementarity to the nucleic acid molecule of (a) or (b).